EXHIBIT 4

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Yale Cancer Center HISTORY AND PHYSICAL (Hofstatter)

12/28/2010

Re: CONVERSE, HILARY [redacted])
MRN: 0318239
Provider: Erin Hofstatter, MD
Date of Service: 12/21/2010

HISTORY AND PHYSICAL

DIAGNOSIS: High risk evaluation for breast cancer, and history of stage I ovarian cancer.

HISTORY OF PRESENT ILLNESS: Hilary Converse is a 62-year-old female with a history of stage IA clear cell ovarian carcinoma at age 58, who presents today for high-risk evaluation for breast cancer. The patient was originally diagnosed with clear cell ovarian cancer, stage IA, in 2007, for which she underwent TAH/BSO and six cycles of carboplatin/Taxol. She has remained free of disease since that time. She is of Ashkenazi Jewish heritage, and met with the genetic counselors at Yale Cancer Center a few years ago, and tested negative for the three common Jewish mutations for BRCA 1 and 2. She has since had full sequencing and BART testing, which also was negative. She does not recall testing for HNPCC. She has previously been followed by Dr. Lannin and most recently has been followed by his surgical PA for breast cancer surveillance. She continues to obtain annual mammograms, most recently done on 11/15/2010, which revealed dense breast tissue bilaterally but no suspicious lesions. She has undergone breast MRI screening in the past, most recently in March 2009. There is an asymmetric parenchymal enhancement in the central right breast, which had been unchanged since April 2008. However, no suspicious findings in the breast bilaterally were noted. The patient was seen in Dr. Lannin's office last week, and she was subsequently referred to this clinic for further discussion of high-risk surveillance.

Symptomatically, the patient has no specific complaints today. She is motivated to pursue breast cancer surveillance as recommended by her providers. She does have chronic pain from a fibromyalgia syndrome but otherwise denies fevers, chills, nausea, vomiting, chest pain, shortness of breath, abdominal pain, dysuria, bowel changes, skin rash, or weight loss.

Of note, the patient provides me with her most recent bone mineral density performed on 10/27/2010, which reveals a T-score of -1.2, following just into the osteopenic region. She also provides me with recent blood tests which reveal BUN 21, creatinine 0.8, alkaline phosphatase 104, AST 25, ALT 22, total bilirubin 0.3, cholesterol 210, HDL 91, and LDL 104.

REVIEW OF SYSTEMS: Please see HPI. Complete review of systems is performed and is otherwise negative.

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BREAST CANCER RISK FACTORS: Menses at age 14. The patient has been menopausal for "several years." She is G2, P2 with parity at age 24. She is of Ashkenazi Jewish heritage and has a positive family history of breast cancer, pancreatic cancer, as well as a personal history of breast cancer as outlined below. The patient drinks three alcohol beverages per week. She has never received radiation therapy to the chest. She has one previous breast biopsy, actually a cyst aspiration in the left breast several years ago. She took birth control pills for approximately 12 years from age 18 to 30. She took estrogen and progesterone hormone replacement therapy for approximately 10 years until 2007.

PAST MEDICAL HISTORY: The patient was diagnosed with stage IA clear cell ovarian carcinoma at age 58, for which she underwent TAH/BSO and received six cycles of carbo/Taxol. She has a history of cystic breasts. Baker's cyst of the right knee, two meniscus tears in the right knee, osteopenia, fibromyalgia, interstitial cystitis, herniated disc status post cervical fusion in 2008, status post trigger thumb surgery, question seizure in 2006, status post foot surgery, and status post adenoid surgery.

MEDICATIONS: Lasix, Klor-Con, Amrex, omega-3, calcium, MOBIC, Nexium, Xanax, hydrocodone, Elmiron, sertraline, multivitamin, Flector patch, Fioricet as need, Vagifem twice a week.

ALLERGIES: Sulfa, scallops, and antibiotic ointment.

FAMILY HISTORY: The patient's mother had breast cancer at age 46, and is alive today at age 90. She did test negative for any genetic mutation. The patient's father had lung cancer at age 85. The patient's maternal grandmother had pancreatic cancer at age 87. The patient's maternal uncle was diagnosed with non-Hodgkin's lymphoma in his 70s. The patient herself has no siblings. The patient's daughter is 37, and has been told that she should have her ovaries removed at age 40.

SOCIAL HISTORY: The patient lives in Prospect. She is married with two children, one daughter and one son. She owns an architectural firm. She is a former smoker approximately one pack per day for 20 years and quit 15 to 20 years ago. She drinks three alcoholic beverages per week. She maintains an active lifestyle.

PHYSICAL EXAMINATION:
Vital Signs: Temperature 98.1 degrees, pulse 98, respirations 18, height 167.6 cm, weight 76.1 kg, blood pressure 143/82, and O2 saturation 100% on room air.
ECOG performance score 0.
Pain score mild to moderate secondary to fibromyalgia.
General: The patient is a well-appearing female in no acute distress. She is alert and oriented x 3. She presents alone today.
HEENT: Extraocular movements intact. Sclerae anicteric. Mucous membranes moist. Pharynx is clear without erythema or exudate.
Neck: Supple.
Nodes: There is no appreciable cervical, supraclavicular, or axillary lymphadenopathy.
Heart: Regular rate and rhythm. Normal S1 and S2. No murmurs, rubs, or gallops.

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Lungs: Clear to auscultation bilaterally.
Abdomen: Soft, nontender, and nondistended. There is no hepatosplenomegaly appreciated.
Extremities: No edema.
Breasts: There are no skin changes, skin dimpling, nipple retraction, nipple discharge, or suspicious masses bilaterally.

ASSESSMENT AND PLAN: Hilary Converse is a 62-year-old female with a personal history of stage IA clear cell ovarian carcinoma at age 58, who presents today for further evaluation regarding high-risk breast cancer surveillance. The patient herself has undergone testing for BRCA 1 and 2, including full sequencing of the genes as well as BART, and this testing has been negative. However, given the patient's personal history of ovarian cancer, as well as a significant family history of young breast cancer in the patient's mother as well as a pancreatic cancer in the patient's maternal grandmother, I do imagine that the patient's family may carry a gene for a hereditary breast/ovarian cancer syndrome that has yet been unidentified. Thus, I do think she merits high-risk surveillance.

It is difficult to precisely estimate the patient's risk of breast cancer over the next 5 to 10 years. Were she a BRCA 1 or 2 carrier, the risk of breast cancer over the next 10 years could be as high as 15% to 25%. Alternatively, the Gail model might predict that the patient's risk of breast cancer over the next five years would be as low as 2.7%, with a lifetime risk at age 90 of approximately 11.8%. However, given the patient's likelihood of having a genetic mutation in her family, I do not think that the Gail model is an appropriate risk estimator for this patient.

In regards to specific recommendations, I will review her case with the genetic counselors regarding any need for additional genetic testing for a gene such as HNPCC. Certainly the patient's ovarian cancer and perhaps the pancreatic cancer in her family may be suggestive of HNPCC, however, breast cancer does not track with Lynch syndrome. I will review her case with the group accordingly.

In regards to surveillance modalities, I certainly recommend annual mammography. The question as to the additional need for either breast ultrasound or breast MRI is a more difficult question to answer. The patient is aware of the potential for false positivity with breast MRI. I do think that breast MRI is better established as opposed to breast ultrasound for screening purposes. I would tend to err on the side of caution and would obtain an annual breast mammography with annual breast MRI staggered by six months, though I will review this with the patient's gynecologist Dr. Fine, as well as with Dr. Lannin's office. In general, the recommendation for routine use of screening breast MRI is usually when the patient's lifetime risk approximately it is 20% to 25%, but again these numbers are difficult to estimate in this patient.

I have also reviewed breast self exam with the patient. I have also recommended that she undergo a clinical breast exam at least twice a year.

In terms of chemoprevention, the patient would be a candidate for breast cancer prevention with tamoxifen. This medication has been shown to reduce a woman's risk of breast cancer by approximately 50%, though the absolute risk reduction is on the order of single digits. I have

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explained in detail both the regimen and side effects of tamoxifen, which will be a five year course of daily tamoxifen therapy with potential side effects including hot flashes, night sweats, leg cramps, blood clots, stroke, and cataracts. The additional risk of uterine cancer does not apply to this patient given her history of TAH/BSO. It may potentially benefit her bones, given her history of osteopenia. I have also reviewed Evista as a possible alternative, though it is felt that Evista is not quite as effective as tamoxifen in terms of breast cancer prevention but may have fewer vasomotor side effects. The patient will think further about this option, and will contact me if she decides she will be interested in pursuing this.

In terms of surgical options, the patient is aware that bilateral prophylactic mastectomy is an option for her though this certainly would be extreme. Nevertheless, bilateral mastectomy is known to reduce the risk of breast cancer by over 90% in BRCA 1 and 2 carriers. The patient is aware that this is an option for her at any time.

Finally, in terms of lifestyle changes, I have advised that she limit her alcohol intake to approximately three alcoholic beverages per week or less. Additionally, I have advised that postmenopausal weight gain has been associated with increased risk of breast cancer. I have advised her to maintain a healthy diet as well as exercise in an effort to minimize any postmenopausal weight gain.

I will be in touch with both the patient's gynecologist Dr. Emily Fine regarding my recommendations as well as with Dr. Lannin's office regarding specific recommendations for breast MRI versus breast ultrasound. I will then be in touch with the patient regarding the team's recommendations and will make appointments accordingly. The patient has my contact information and knows to contact me in the interim. Otherwise, I will be happy to follow the patient clinically, in conjunction with Dr. Lannin's office as well as with Dr. Fine.

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Erin Hofstatter, M.D.
Assistant Professor of Medicine

Dictated By: Erin Hofstatter

Signed By: Erin Hofstatter, MD Dec 28 2010 5:00PM

cc:
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